

1006-43

Hirulog™ vs. Heparin During Percutaneous Transluminal Coronary Angioplasty in Patients with Post-Infarction Angina: Results of the Myocardial Infarction Arm of the Hirulog Angioplasty Trial

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Acute intervention for recurrent angina following an acute myocardial infarction continues to present as a therapeutic challenge to the physician. Standard anticoagulation using heparin during PTCA in patients with post infarction angina is associated with a 16% incidence of abrupt vessel closure and an 11% incidence of death, CABG, and recurrent MI. The ability of Hirulog™ (BG8967), a direct thrombin inhibitor, to improve PTCA outcome was compared in a double blind fashion to heparin in the Phase III Hirulog Angioplasty Trial. Clinical and angiographic results from the post infarction subgroup (n = 635) will be reported. Patients were randomized to either Hirulog™ (2.2 mg/kg bolus and 1.0 mg/kg/hr infusion) or heparin (175 U/kg bolus and 15 U/kg/hr infusion). Additional boluses were administered in order to maintain a minimum activated clotting time of 350 seconds. The primary endpoint was procedural failure (impending or established abrupt vessel closure, bypass surgery, recurrent MI, or death) with a secondary endpoint of major hemorrhage. The event rates in this 635 patient subgroup were: Death 0.8% (n = 5), Emergency Bypass 2.2% (n = 14), Recurrent Myocardial Infarction 2.5% (n = 16), Abrupt vessel closure 5.8% (n = 37), and Major Hemorrhage 6.8% (n = 43).

In summary, this study will determine: (1) whether Hirulog™, a direct thrombin inhibitor, is superior to heparin when used during PTCA in patients with post-infarct angina and (2) the overall safety profile of Hirulog™ in this subgroup.

1006-44

A Prognostic Factor in Coronary Artery Disease (CAD): Platelet-Dependent Thrombin Generation in Patients with CAD

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We examined platelet-dependent thrombin generation in patients with coronary artery disease (CAD). Thrombin generation was measured according to the method of Aronson et al (Circulation, 1992). 0.5 ml of platelet rich plasma (PRP, 15×10^4 /ml) was prepared, and 40 mM of CaCl₂ was added to start clotting. 0.5 mM of S-2238 was added to each sample in a microtiter plate every 10 min, and the plate was read kinetically at a wavelength of 405 nm on a microtiter plate reader. The patients with CAD divided into 3 groups.

Thrombin generation 20 min after CaCl₂ addition is:

Control (n = 12)	48 ± 10(mOD)
Stable angina (SAP) (n = 15)	79 ± 27
Unstable angina (UAP) (n = 15)	**562 ± 155
Acute myocardial infarct (AMI) (n = 43)	**440 ± 269

**p < 0.01 compared to SAP

The patients with UAP and AMI showed marked increase in thrombin generation compared to SAP and control subjects. AMI patients with severe coronary artery disease (Group B) showed higher levels of thrombin generation (Group A, Gensini score < 32: 382 ± 248 mOD vs Group B, Gensini score > 31: 578 ± 238 , P < 0.05). LVEF of group A is significantly higher than that of group B (P < 0.05). These findings indicate that patients with UAP and AMI have an evidence of hypercoagulable states and that platelet-dependent thrombin generation may play an important role in pathophysiology of UAP or AMI, and may be a prognostic factor in CAD.

1006-45

Regression of Infarct-Related Coronary Lesions on Aggressive Lipid Lowering Treatment in Patients After Recovery from Acute Myocardial Infarction

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Considering of remained active nature of infarct-related lesion (IRL) early after recovery from acute myocardial infarction (AMI), a prospective study was undertaken to determine whether IRL exhibits more regression on aggressive lipid lowering treatment. Fifty patients (pts), 34 hyperlipemic (HL) and 16 normal lipids (NL), aged ≤ 65 years with coronary diameter stenosis >25% were followed monthly. LDL-cholesterol (LDL-C) level was aimed to control below 130 mg/dl in HL patients on strict diet and pravastatin 10–30 mg/day, also LDL-apheresis in a patient with familial hyperlipemia. Repeat coronary angiography was performed in average 14 months after AMI onset, and al-

together 142 lesions from 34 HL and 16 NL were analyzed quantitatively using cine-densitometry. Lesions which PTCA wire crossed were separately assessed. Average serum LDL-C levels improved from 166 to 117 mg/dl on drug and diet (p < 0.001) in HL. Seven out of 92 non-IRL (7.6%) exhibited progression defined as ≥0.5 mm decrease of minimum lesion diameter, and 9 IRL (9.8%) did regression ≥0.5 mm increase. Whereas thirty five IRL showed significantly more incidence of regression (9 sites, 25.7% p = 0.021) and similar rate of progression (3 pts, 8.6%). An improvement of LDL-C/HDL-C ratio was more prominent in patients with IRL regression compared with those showing progression or no change (p < 0.05).

Thus the IRL was found in favor of more regression than non-IRL, and the magnitude of lesion regression can be expected according to the effect of lipid lowering treatment in patients after AMI.

1007

Pericardial Physiology and Pathology; Cardioversion; Diastolic Function; Thyrotoxicosis

Wednesday, March 22, 1995, Noon–2:00 p.m.

Ernest N. Morial Convention Center, Hall E

Presentation Hour: 1:00 p.m.–2:00 p.m.

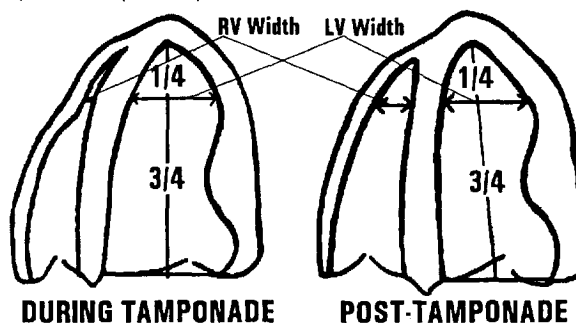
1007-16

Quantitation of Apical Right Ventricular Collapse in Tamponade: A Diagnostic Improvement

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Right ventricular (RV) collapse, a popular echocardiographic sign of tamponade is a subjective call with no precise criteria. RV collapse is usually diagnosed by early diastolic "dimpling" or local concavity of RV anterior wall in parasternal views. In 15 patients with pericardial effusion studied (A) during tamponade, and (B) after relief of tamponade, we noted that definite such "dimpling" could be seen in only five out of ten cases, while in six patients parasternal window was inadequate. In contrast, the apical four-chamber view could be obtained in all 15 patients. In this view we made several RV measurements including various transverse RV dimensions, RV area and ratios of these to the corresponding LV measurements.

Results: LV width/RV width ratio at the junction of the apical 1/4 to basal 3/4 of LV length showed the best separation between tamponade and post-tamponade values (p < 0.005). Using a cut-off value of LV width/RV width ≥3 as indicative of tamponade. This criterion showed no overlap between tamponade and post-tamponade values.



Conclusion: Ratio of LV width to RV width ≥3, measured at the junction of apical 1/4 with basal 3/4 of LV, is a promising sign of tamponade, reflecting selectively greater collapse of near-apical region of RV in tamponade.

1007-17

Demonstration of Pericardial Constraint in Chronic Heart Failure

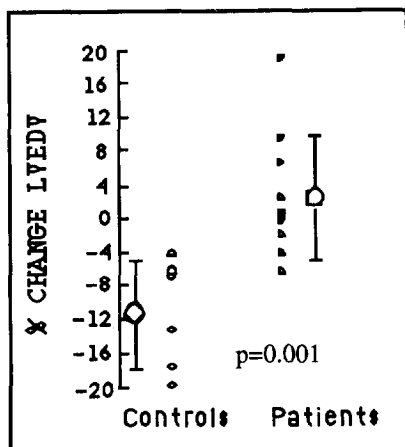
John J. Atherton, Suhas S. Lele, Helen L. Thomson, Karen N. Wright, Gerry W.F. Muehle, Thomas Moore, Israel Belenkie, Andrew J. Galbraith, John V. Tyberg, Michael P. Frenneaux. *Departments of Medicine, University of Queensland, Australia; University of Calgary, Canada*

Pericardial constraint may be an important feature in chronic heart failure (CHF). We hypothesized that baseline pericardial constraint could be inferred if left ventricular end-diastolic volume (LVEDV) paradoxically increased during lower body negative pressure (LBNP), as a consequence of abolition of constraint with an increase in the left ventricular transmural and transeptal pressure gradients.

Methods: 11 patients with CHF and left ventricular ejection fraction <35% (age 34–82, mean 51.5 years; 8 male, 3 female) were compared with 6 healthy controls (age 31–61, mean 50.5 years; all male). Radionuclide ven-

tricolography was performed before and during application of 30 mmHg LBNP. Left ventricular end-diastolic counts were corrected for time decay and tissue attenuation. LVEDV was then calculated with reference to an externally counted blood sample taken during each of the acquisitions.

Results (expressed as mean \pm SD): Comparing baseline with 30 mmHg LBNP, LVEDV changed by -4.5 to -26.3 ml (mean -14.2 ± 8.6 ml) in controls vs. -24.4 to $+62.1$ ml (mean $+8.2 \pm 23.5$ ml) in CHF patients ($p = 0.04$). The % change in LVEDV with LBNP (mean \pm SD) is shown in the figure. There was a linear correlation between change in LVEDV and baseline pulmonary capillary wedge pressure (b-PCWP) in CHF patients ($r = 0.68$; $p = 0.03$).



Conclusions: Baseline pericardial constraint is demonstrated in the 4 patients with CHF in whom LVEDV increased during LBNP, a response associated with higher b-PCWP. In patients with attenuated reductions in LVEDV, abolition of baseline constraint and impaired myocardial compliance are both possible explanations.

1007-18

Tumor Markers in Differential Diagnosis of Pericardial Effusions of Different Etiologies

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Methods. Diagnostic and therapeutic pericardiostomy with drainage and biopsy was performed and then adenosine deaminase (ADA) and carcinoembryonic antigen (CEA) levels were measured in the pericardial fluid in 36 patients (pts) with moderate to large pericardial effusion (PE) and 19 control pts. Carbohydrate antigen 19-9 (CA 19-9) and ferritin were also measured in some pts. Pts were included in a prospective protocol from August, 1991 to July, 1994 and grouped as follows: Group I — 11 pts with tuberculous pericarditis (TP); Group II — 6 pts with clinically strongly suspected TP; Group III — 22 pts with malignancy (15) and acute pericarditis (7); Group IV — 19 control pts without pericardial disease. We observed any symptoms and signs of recurrent pericarditis or constrictive pericarditis on follow-up.

Results. 1) In group I (99 ± 11 U/L) and group II (77 ± 27 U/L), the ADA activity was significantly higher than that in group III (18 ± 3 U/L) or that in group IV (18 ± 2 U/L) ($p < 0.05$). 2) With a cutoff value for ADA activity of 40 U/L, sensitivity was 94% and specificity 96% in the diagnosis of TP. 3) In benign diseases, the CEA level was significantly lower (1.89 ± 0.50 ng/ml) than that in malignant diseases (194.53 ± 59.05 ng/ml) ($p < 0.05$). 4) With a cutoff value for CEA level of 5 ng/ml, the sensitivity is 80% and specificity is 96% in the diagnosis of malignant pericarditis. 5) The value of CA 19-9 and ferritin was lower than that of ADA and CEA. 6) Follow-up study (mean, 19.5, 29.0, 11.8 months in groups I, II, and III, respectively) showed no symptoms and signs of constrictive pericarditis except two pts.

Conclusions. Pericardial fluid ADA and CEA are useful for the differential diagnosis of pericardial effusion of various causes.

1007-19

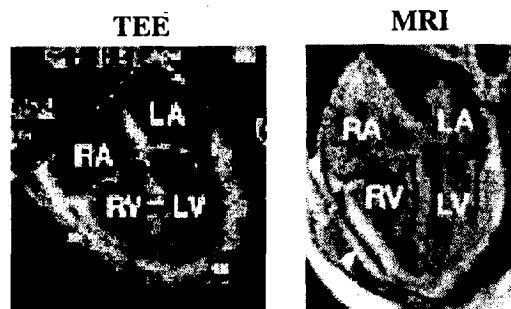
Transesophageal Echocardiography is a Useful Technique in Localizing Pericardial Thickening in Patients with Diastolic Dysfunction Compared to Magnetic Resonance Imaging

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Transesophageal echocardiography (TEE) has been used to differentiate constrictive pericarditis (CP) from restrictive cardiomyopathy (RCM) by Doppler

echocardiography; however its utility to anatomically localize pericardial thickening (PT) has not been described. We prospectively studied 62 patients with clinically suspected diastolic dysfunction with both TEE and magnetic resonance imaging (MRI), and detected 35 patients (29 M; mean age 59 ± 14 yrs.) with pericardial disease (surgically confirmed, $n = 13$) and compared the location PT independently. Fourteen pts. had CP; 6 had effusive-CP and 15 had mixed CP/RCM. PT location was graded independently as predominantly involving the right heart (RT), left heart (LT), generalized (GE) or no thickening (NO).

(pts)	TEE			
	RT	LT	GE	NO
MRI				
RT	0	0	0	0
LT	0	0	2	1
GE	0	0	30	0
NO	2	0	0	0



TEE and MRI were in agreement in 30 (86%) of 35 patients (concordance $> 70\%$; $p = 0.05$). TEE was able to visualize PT adjacent to the right ventricular apex and left ventricular apex but TEE was limited in visualizing the lateral LV wall. **Conclusions:** TEE and MRI are concordant in localizing pericardial thickening in pts with diastolic dysfunction. These findings suggest that TEE, when combined with Doppler flows, provides an excellent technique in the diagnosis of constrictive pericarditis.

1007-20

Myocardial Protection in Electrical Cardioversion. The Importance of Magnesium and Creatinine Phosphate

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Transient elevation of serum enzyme level, abnormalities of repolarisation and arrhythmias following electrical cardioversion (EC) are usually observed. We aimed to alleviate these alterations by pre treatment with magnesium sulphate (Mg) and/or creatinine phosphate (Neoton). The study group consist of 80 patients (pts) mean age 48 ± 8 years who had EC (300V) for chronic atrial fibrillation (AF) after mitral and/or aortic valve surgery. They were randomly divided into subgroups: 20 pts in whom Mg was administrated i.v. (100 mg/kg b.w.) before EC; 20 pts who received Neoton i.v. in the following mode — 4 g before EC and 4 g in the first 12 hours after EC; 20 pts who received Mg and Neoton in the same doses and 20 control subjects. Total serum magnesium level and CK-MB level were recorded before and 8 hours after EC. Recovery to sinus rhythm (SR), ST segment shifts were recorded immediately before and after EC. Supraventricular (SV) and ventricular premature beats (VPB) were studied with 24 hour Holter monitoring.

	Mg	Neoton	Mg + Neoton	Control
CK-MB (μ l)	$3.8 \pm 1.3^{**}$	$4.1 \pm 1.8^{**}$	$4.5 \pm 1.5^{**}$	10 ± 13
Mg (mmol/l)	$1.18 \pm 0.42^*$	$1.15 \pm 0.20^*$	$1.36 \pm 0.51^*$	1.98 ± 0.63
SR (%)	70 NS	71 NS	77 NS	67 NS
ST changes (mm)	$1.34 \pm 0.89^{**}$	$1.28 \pm 0.76^{**}$	$1.23 \pm 0.81^{**}$	2.92 ± 1.67
SV	968 ± 920	821 ± 760	$403 \pm 563^*$	704 ± 803
VPB	$39 \pm 82^*$	165 ± 108	$89 \pm 78^*$	275 ± 201

* $p < 0.05$, ** $p < 0.01$ as compare to control; all values after EC

Our results suggest that Mg, creatinine phosphate or both administrated before EC have significant cardioprotective effect.

1007-21

Effects of Changes in Atrioventricular Gradient and Isovolumic Relaxation Rates on Radionuclide Diastolic Filling in Man

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The relative influences of the left atrioventricular gradient (AVG) and the